



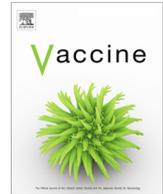
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Commentary

Playing vaccine roulette: Why the current strategy of staking everything on Covid-19 vaccines is a high-stakes wager



Elisabeth Paul ^{a,*}, Garrett W. Brown ^b, Andreas Kalk ^c, Valéry Ridde ^d

^a Université libre de Bruxelles, School of Public Health, Campus Erasme, Route de Lennik 808, CP 591, 1070 Brussels, Belgium

^b University of Leeds, Global Health Theme, POLIS, Leeds, United Kingdom

^c Deutsche Gesellschaft für Internationale Zusammenarbeit, Kinshasa Country Office, Kinshasa, The Democratic Republic of the Congo

^d Institut de Recherche pour le Développement (IRD), CEPED (IRD-Universités de Paris), INSERM, Paris, France

1. Introduction

Many high-income countries and international institutions have bet the proverbial farm on the quick development of a vaccine to respond to the Covid-19 pandemic, implementing measures such as lockdowns and personal restrictions as delaying options while waiting for the vaccine –with enormous collateral damage in terms of increased poverty, intra-familial violence, mental health, undiagnosed health conditions, poor follow-up or lack of treatment [1]. By early July 2021, it was estimated that US \$12.445 billion had already been awarded for vaccine development, a large part from public resources [2]. International Covid-19 funding was overwhelmingly dedicated to vaccines, at the expense of other strategies. Take the example of the Access to Covid-19 Tools (ACT) Accelerator, a ‘global collaboration of the world’s top international health organisations working together to accelerate the development, production, and equitable delivery of Covid-19 tests, treatments, and vaccines’. The overall aim of ACT-A is ‘to speed up an end to the pandemic by supporting the development and equitable distribution of the tests, treatments and vaccines the world needs’. As of 9 July 2021, public and private donors had already pledged over US\$12.2 billion to COVAX (the vaccines pillar of the (ACT) Accelerator) [3]. By contrast, very little has been invested in the search for treatment, or for health system strengthening, or system readiness, especially in terms of enhancing primary care, human resources, and training.

Table 1 shows the estimated needs (targets) and pledges to the ACT Accelerator along its four pillars as of 9 July 2021. The vaccine pillar received 84% of confirmed financing, leaving the pillar with a gap of 7% of estimated needs. This contrasts with the three other pillars, which face a funding gap of 82% (therapeutics), 89% (diagnostics) and 91% (health system) of needs, respectively. What this suggests is that the Covid-19 response policy remains fixated on vaccines, where all other bets are off.

Here, we do not question the principle of immunisation, particularly immunisation that prevents disease transmission and

infection, which has led to undisputable successes in many areas and is, overall, ‘one of the best health investments money can buy’ [4]. Moreover, it would be churlish to dismiss the unprecedented feat and pace of development of anti-Covid-19 vaccines. The vaccines approved to date have proven to be safe and very effective – at least in the short run [5–10]. This gives the world hope that the pandemic can ultimately be controlled.

Yet, at this point, we do not readily accept the majority narrative that we’ve hit the jackpot through vaccines. Here, we argue that the current strategy of staking everything on vaccines, without sufficient hindsight on its risk-benefit ratio, and at the expense of complementary strategies (treatment, health system strengthening, non-pharmaceutical prevention, promotion of safe conditions that prevent transmission, and healthy lifestyles), was – and may still remain – insufficient, reactive, short-sighted, and an unnecessary high-stakes wager that is tempting fortune. Below, we highlight a number of limitations of the ‘vaccine-focused’ strategy, and discuss the lack of complementary strategies. We conclude by proposing avenues for designing a more balanced and risk-adverse Covid-19 response policy.

2. Remaining uncertainties about the vaccine gamble

First, many unknowns remain as for the medium-term performance, including sustainability, of the Covid-19 vaccine strategy. The efficacy of candidate vaccines has been determined through randomised controlled clinical trials (RCTs), coined the gold standard in clinical designs for their high internal validity. Yet, context is essential when interpreting the results of any randomised trial [11] because no intervention acts on two persons in an identical fashion, and results are influenced by individual risk factors [12]. Moreover, the criteria used by clinical trials to evaluate Covid-19 vaccine efficacy were not fully relevant for managing the pandemic [13,14]. Considering the extremely diverse patterns of SARS-CoV-2 epidemiology, it is feasible that RCTs are limited in their capacity to comprehend the complexity of the interaction between each patient, their immune system, and the vaccine. As a result, policy that bets heavily on post-facto pandemic vaccine discovery, RCTs, and expedited approval processes, risk to be too standardised to

* Corresponding author.

E-mail addresses: Elisabeth.Paul@ulb.be (E. Paul), G.W.Brown@leeds.ac.uk (G.W. Brown), andreas.kalk@giz.de (A. Kalk), valery.ridde@ird.fr (V. Ridde).

Table 1

Estimated needs and commitments to the four arms of the ACT Accelerator as of 19 February 2021. Source: Authors, based on ACT-Accelerator Commitment Tracker [3].

Billion US\$	Diagnostics Pillar	Therapeutics Pillar	Health Systems Connector	Vaccine Pillar
Revised Budget, 12 March 2021 (% of total)	9.7 (29%)	3.9 (12%)	7.9 (24%)	11.7 (35%)
Confirmed (% of total)	1 (7%)	0.8 (6%)	0.6 (4%)	12.2 (84%)
Gap (% of budget)	89%	82%	91%	7%

accommodate for various subgroups' specificities, like pregnant women or ethnic minorities [15,16], and therefore risks being sub-optimal. As one example, problems have emerged for people with serious allergies, who were vaccinated with severe side-effects, but who were later discovered to be excluded from the Pfizer clinical trials, leaving clinicians in the UK unprepared [17].

We contend that the precautionary principle should be applied since the balance between the risks and benefits of SARS-CoV-2 infection vs. new vaccines is not only largely unknown over the medium term, but also extremely variable, in the short term. For example, variability from one age decadal to another, from one individual to another (with differential expected risks from Covid-19 – thus, expected vaccine benefits – sometimes bigger than 10,000 to 1) – and even from one vaccine to another [18]. Most infected people do not develop symptoms and, although we do not yet know the long term implications of infection, it is estimated that Covid-19 infection fatality rates in people under 70 years of age turns around 0.05% [19]. Immunisation is generally justified on the grounds of preventing transmission to a significant share of susceptible groups and as a means to ensure herd immunity. Even if preliminary data from several countries are quite encouraging [20–22], it is still unclear whether the Covid-19 vaccines will deliver the outcomes that really matter, namely, long-lasting protection, reduction in mortality and the occurrence of transmission (for herd immunity) [13,23]. In the case of Pfizer and Moderna, the vaccine trials were unable to determine the exact duration of immunity to severe disease beyond six months nor the potential frequency of additional booster doses (Pfizer has already started to suggest that boosters are needed just eight months since mass vaccinations began), representing a further gamble within a process where there are concerns about protocol adherence, data quality, proper reporting and overall effectiveness [15]. There are already indications that current vaccines are less effective against some SARS-CoV-2 variants [24,25], that countries with high vaccination coverage may still experience surges in SARS-CoV-2 infections [26], and that herd immunity may not be reached [27]. This is of particular concern for vaccines that could entail short-term risks and long-term adverse impacts [28], especially due to the fact that gene therapy vaccines are new platforms, not yet tested through mass vaccination campaigns.

We also contend that given the unknowns about the potential of Covid-19 vaccines to be effective against variant strains, to reduce mortality, and to prevent transmission – whereas long-term adverse effects of these vaccines are also unknown – there are arguments to pursue an immunisation policy that is targeted on high-risk populations (e.g. old people, people with comorbidities and healthcare workers), rather than mass vaccination campaigns. This also means avoiding copy-paste vaccination policies from other countries, rather adapting policy to each context in terms of population structure, vaccine acceptance, system capacities and epidemic timing [29].

Given the complexities in sense-making, it is curious to observe how immediate claims in vaccine safety have been made – with assertions as strong as “there is no question that the current vaccines are effective and safe” [30] – while vaccine hesitation is high worldwide [31], while some rare scientists warn against potential negative side-effects [28,32] and while, by definition, with such a short observation period, no one actually has any idea of

medium- and long-term effects of Covid-19 vaccines. This threatens to escalate knock-on risks associated with public vaccine hesitancy – which is already present with Covid-19 vaccines [33,34], but which could also spill over to undermine trust in other well-proven, effective and efficient vaccines.

3. Need of complementary strategies

Beyond the questions about efficacy, a particularly worrying gamble relates to real-life vaccine effectiveness and equity. This is because it is one thing to create a vaccine and quite another to manufacture, distribute and effectively administer the vaccine at scale, especially in a way that is equitable. Our over-reliance on vaccine discovery has now revealed serious concerns about Covid-19 vaccine access, manufacturing, cold-chain storage, distribution, system readiness, vaccine nationalism, and acceptability. In many ways it is reasonable to envision that vaccine distribution and logistics, human resource capacities, the governance of programs, and conditions of access, will become the biggest global health governance challenge for the foreseeable future, overshadowing more balanced and holistic approaches to public health (as witnessed at the last Government of Seven G7 Summit). Yet, as illustrated above with ACT-A, insufficient funding has been dedicated at the global level to sustain health systems.

Moreover, in many countries the Covid-19 response was elaborated without properly evaluating the real threat of the pandemic on different populations (age groups, etc.), without appropriately targeting vulnerable populations, without taking sufficient account of the harms of restrictions imposed while waiting for vaccines to be delivered [35–37], and without taking account of long-proven public health and health promotion experience [38]. In particular, Covid-19 response has focused on virus control, paying insufficient attention to other factors such as social determinants, age, comorbidities, and previous exposure to a certain range of infections [39], which play a determining role in explaining the ‘transition’ from SARS-CoV-2 infection to severe forms of Covid-19 [40]. In terms of hedging one's bet, overextending a single wager within a complex problem like Covid-19 undermines efficiency [41]. In terms of a preparedness strategy, reliance on this paradigm becomes increasingly high-stakes as the risks from emerging epidemics and syndemics are estimated to intensify with increased habitat encroachment, intensifying social inequality, degradation of living, social environments and ecologies, urban density, and climate change [42,43].

4. Conclusion: Hedging one's bets

We have argued that the current strategy of staking everything on the vaccine, however successful it looks today, was a risky and insufficient strategy. Instead of gambling everything on vaccine strategies, we call for adopting a more holistic and diversified response to both the current Covid-19 pandemic and future disease preparedness. One that hedges its bet on a continuum of strategies including health promotion and healthy lifestyles [38], targeted prevention of other determinants of health (e.g., nutritional deficiencies [44]), adequate primary care and early treatment (especially now that we have a more evidence of effective

or promising treatments [45–47]), health system strengthening [48], and sufficient national, regional and global system policy preparedness for emerging epidemics, enabling to build “pandemic proof health systems” [49]. In particular, vaccination strategies need to be more nuanced and targeted, and new Covid-19 vaccines need to be configured within an overall public health strategy that will differ in profile for different countries. Strategies should also consider the already acquired natural immunity amongst those that have been infected [50,51]. An optimal mix of policies should be chosen according to a careful risk-benefit assessment, adopting the precautionary principle to new vaccines, and ensuring public health policy coherence. At the global level, such an approach also includes appropriate financing of the other ACT pillars in the short-term. None of this precludes publicly pooled and coordinated investments in vaccine development and use, since effective vaccines when embedded within the aforementioned health continuum will have far better odds of hitting a health jackpot. Nevertheless, it does preclude continuance of the current policy and the mess we find ourselves in, which is to wait for acute health emergencies, to implement delay tactics, while staking everything on a spin of the vaccine roulette.

5. Authorship

EP had the initial idea of this paper. EP and GWB wrote the first draft. All authors contributed to deepening the analysis and reviewing the drafts, and approved the final draft.

Funding

None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] Collateral Global. A regular publication analysing the global impact of COVID-19 restrictions [Internet]. Available from: <https://collateralglobal.org/>.
- [2] PharmaNews. COVID-19 Vaccine Dashboard [Internet]. 2021 [cited 2022AD Jul 12]. Available from: <https://pharmanews.linksbridge.com/Covid-19>.
- [3] World Health Organization. Access to COVID-19 tools funding commitment tracker [Internet]. 2021 [cited 2021 Jul 12]. Available from: <https://www.who.int/publications/m/item/access-to-covid-19-tools-tracker>.
- [4] World Health Organization. Vaccines and immunization [Internet]. Available from: https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_1.
- [5] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383(27):2603–15.
- [6] Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med* 2021;384(5):403–16.
- [7] Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet* 2021;397(10269):99–111.
- [8] Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med* 2021;384(23):2187–201.
- [9] Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. *JAMA* 2021;326(1):35–45.
- [10] Logunov DY, Dolzhenkova IV, Shchelyakov DV, Tukhvatulin AI, Zubkova OV, Dzhurullayeva AS, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *The Lancet* 2021;397(10275):671–81.
- [11] Craig P, Di Ruggiero E, Frohlich K, Mykhalovskiy E, White M. Taking account of context in population health intervention research: guidance for producers, users and funders of research [Internet]. Southampton: on behalf of the Canadian Institutes of Health Research (CIHR)–National Institute for Health Research (NIHR); 2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK498645/pdf/Bookshelf_NBK498645.pdf.
- [12] Harrington DP, Baden LR, Hogan JW. A large, simple trial leading to complex questions. *N Engl J Med* 2020(Dec). <https://doi.org/10.1056/NEJMe2034294>.
- [13] Doshi P. Will covid-19 vaccines save lives? Current trials aren't designed to tell us. *BMJ* 2020;21(371):m4037.
- [14] Doshi P. Clarification: Pfizer and Moderna's “95% effective” vaccines—we need more details and the raw data [Internet]. *The BMJ Opinion*. 2021 [cited 2021 Apr 12]. Available from: <https://blogs.bmj.com/bmj/2021/02/05/clarification-pfizer-and-modernas-95-effective-vaccines-we-need-more-details-and-the-raw-data/>.
- [15] Ledford H, Cyranoski D, Van Noorden R. The UK has approved a COVID vaccine - here's what scientists now want to know. *Nature* 2020;588(7837):205–6.
- [16] Flores LE, Frontera WR, Andrasik MP, del Rio C, Mondríguez-González A, Price SA, et al. Assessment of the inclusion of racial/ethnic minority, female, and older individuals in vaccine clinical trials. *JAMA Netw Open* 2021;4(2):e2037640.
- [17] Associated Press. Britain investigates possible allergic reactions to Pfizer's COVID-19 shot. *Los Angeles Times* [Internet]. 2020 Dec 9; Available from: <https://www.latimes.com/world-nation/story/2020-12-09/uk-investigates-possible-allergic-reactions-covid-19-vaccine>.
- [18] Ledford H. Why COVID vaccines are so difficult to compare. *Nature* 2021;591(16–17). , <https://www.nature.com/articles/d41586-021-00409-0>.
- [19] Ioannidis JPA. Infection fatality rate of COVID-19 inferred from seroprevalence data. *Bull World Health Organ* 2020. , https://www.who.int/bulletin/online_first/BLT.20.265892.pdf.
- [20] Mallapaty S. Vaccines are curbing COVID: Data from Israel show drop in infections. *Nature* 2021;590(197). , https://www.nature.com/articles/d41586-021-00316-4?utm_source=Nature+Briefing&utm_campaign=700127432c-briefing-dy-20210205&utm_medium=email&utm_term=0_c9dfd39373-700127432c-45689842.
- [21] Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile [cited 2021 Jul 12]. *N Engl J Med* 2021. <https://doi.org/10.1056/NEJMoa2107715>.
- [22] Keehner J, Horton LE, Pfeffer MA, Longhurst CA, Schooley RT, Currier JS, et al. SARS-CoV-2 infection after vaccination in health care workers in California. *N Engl J Med* 2021;384(18):1774–5.
- [23] Mallapaty S. Can COVID vaccines stop transmission? Scientists race to find answers. *Nature* 2021(Feb).
- [24] Bailly B, Guilpain L, Bouiller K, Chirouze C, N'Debi M, Soulier A, et al. BNT162b2 mRNA vaccination did not prevent an outbreak of SARS COV-2 variant 501Y.V2 in an elderly nursing home but reduced transmission and disease severity. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2021(May).
- [25] Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. *N Engl J Med* 2021;384(20):1885–98.
- [26] Ledford H. Six months of COVID vaccines: what 1.7 billion doses have taught scientists. *Nature* 2021;594(164–167). , https://www.nature.com/articles/d41586-021-01505-x?utm_source=Nature+Briefing&utm_campaign=6b35e184ca-briefing-dy-20210607&utm_medium=email&utm_term=0_c9dfd39373-6b35e184ca-45689842.
- [27] Aschwanden C. Five reasons why COVID herd immunity is probably impossible. *Nature* 2021;591(520–522). , <https://www.nature.com/articles/d41586-021-00728-2>.
- [28] Kostoff RN, Kanduc D, Porter AL, Shoenfeld Y, Calina D, Briggs MB, et al. Vaccine- and natural infection-induced mechanisms that could modulate vaccine safety. *Toxicol Rep* 2020;7:1448–58.
- [29] Domingo Esteban, Perales Celia, Sandri-Goldin Rozanne M. The Time for COVID-19 Vaccination. *J Virol* 2021 25 March; 95(8):e02437–20.
- [30] Rimmel A. COVID vaccines and safety: what the research says. *Nature* 2021;590(538–540). , https://www.nature.com/articles/d41586-021-00290-x?utm_source=Nature+Briefing&utm_campaign=5eb3714930-briefing-dy-20210217&utm_medium=email&utm_term=0_c9dfd39373-5eb3714930-45689842.
- [31] Rodriguez Mega E. Trust in COVID vaccines is growing. *Nature* 2021. , <https://www.nature.com/articles/d41586-021-00368-6>.
- [32] Cardozo T, Veazey R. Informed consent disclosure to vaccine trial subjects of risk of COVID-19 vaccines worsening clinical disease. *Int J Clin Pract* 2020; e13795.
- [33] Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, et al. Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. *Eur J Health Econ* 2020;21(7):977–82.
- [34] Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. A global survey of potential acceptance of a COVID-19 vaccine. *Nat Med* 2020(Oct). <https://doi.org/10.1038/s41591-020-1124-9>.
- [35] McCartney M. We need better evidence on non-drug interventions for covid-19. *BMJ* 2020;370(Sep):m3473.
- [36] Bavli I, Sutton B, Galea S. Harms of public health interventions against covid-19 must not be ignored. *BMJ* 2020;371(Nov):m4074.
- [37] Turcotte-Tremblay A-M, Gali Gali IA, Ridde V. The unintended consequences of COVID-19 mitigation measures matter: practical guidance for investigating them. *BMC Med Res Methodol* 2021;21(1):28.

- [38] Cambon L, Bergeron H, Castel P, Ridde V, Alla F. When the worldwide response to the COVID-19 pandemic is done without health promotion. *Glob Health Promot* 2021;28(2):3–6.
- [39] Nelde A, Bilich T, Heitmann JS, Maringer Y, Salih HR, Roerden M, et al. SARS-CoV-2-derived peptides define heterologous and COVID-19-induced T cell recognition. *Nat Immunol* 2021;22(1):74–85.
- [40] Paul E, Brown GW, Kalk A, Van Damme W, Ridde V, Sturmberg JP. “When My Information Changes, I Alter My Conclusions”. What Can We Learn from the Failures to Adaptively Respond to the SARS-Cov-2 Pandemic and the Under Preparedness of Health Systems to Manage COVID-19? *Int J Health Policy Manag* 2020.
- [41] Sturmberg JP. Health system redesign. How to make health care person-centered, equitable, and sustainable. Cham, Switzerland: Springer; 2018.
- [42] Whitmee S, Haines A, Beyrer C, Boltz F, Capon AG, de Souza Dias BF, et al. Safeguarding human health in the Anthropocene epoch: report of The Rockefeller Foundation-Lancet Commission on planetary health. *The Lancet* 2015;386(10007):1973–2028.
- [43] Swinburn BA, Kraak VI, Allender S, Atkins VJ, Baker PI, Bogard JR, et al. The global syndemic of obesity, undernutrition, and climate change: the lancet commission report. *Lancet Lond Engl* 2019;393(10173):791–846.
- [44] Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of Vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Netw Open* 2020;3(9). e2019722.
- [45] Vaughn VM, Yost M, Abshire C, Flanders SA, Paje D, Grant P, et al. Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19. *JAMA Netw Open* 2021;4(6). e2111788.
- [46] The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19: A Meta-analysis. *JAMA* [Internet]. 2021 Jul 6 [cited 2021 Dec 7]; Available from: <https://doi.org/10.1001/jama.2021.11330>.
- [47] Hill A, Garratt A, Levi J, Falconer J, Ellis L, McCann K, et al. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection. *Open Forum Infect Dis* [Internet]. 2021 Jul 6 [cited 2021 Dec 7];(ofab358). Available from: <https://doi.org/10.1093/ofid/ofab358>.
- [48] Hipgrave DB, Kampo A, Pearson L. Health systems in the ACT-A. *The Lancet* 2021;397(10280):1181–2.
- [49] Michel J, Sauter TC, Tanner M. What does a pandemic proof health system look like? *Glob Health Action* 2021;14(1):1927315.
- [50] Wang Z, Yang X, Zhong J, Zhou Y, Tang Z, Zhou H, et al. Exposure to SARS-CoV-2 generates T-cell memory in the absence of a detectable viral infection. *Nat Commun* 2021;12(1):1724.
- [51] He Z, Ren L, Yang J, Guo L, Feng L, Ma C, et al. Seroprevalence and humoral immune durability of anti-SARS-CoV-2 antibodies in Wuhan, China: a longitudinal, population-level, cross-sectional study. *The Lancet* 2021;397(10279):1075–84.